ANTIDIARRHOEAL ACTIVITY OF *KEDROSTIS FOETIDISSIMA* LEAF EXTRACT ON EXPERIMENTALLY INDUCED DIARRHOEA IN MICE

A Dissertation submitted to
THE TAMIL NADU Dr. M.G.R. MEDICAL UNIVERSITY
CHENNAI – 600 032

In partial fulfillment of the requirements for the award of the Degree of
MASTER OF PHARMACY
IN
BRANCH – IV – PHARMACOLOGY

Submitted by
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Under the guidance of
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OCTOBER 2016

NANDHA COLLEGE OF PHARMACY

(Approved by Govt. of Tamilnadu, AICTE, New Delhi, Recognized by Pharmacy Council of India, New Delhi,
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Date ..... 09.09.2016 .....

CERTIFICATE

This is to certify that the work embodied in this thesis entitled **"ANTIDIARRHOEAL ACTIVITY OF KEDROSTIS FOETIDISSIMA LEAF EXTRACT ON EXPERIMENTALLY INDUCED DIARRHOEA IN MICE"** submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai, was carried out by **Mr. SIVAPRAKASH.V.** in the Department of Pharmacology, Nandha College of Pharmacy, Erode-52 for the partial fulfillment for the degree of **MASTER OF PHARMACY** in Pharmacology under the supervision of **Dr.S.SENGOTTUVELU, M.Pharm., Ph.D.,** Professor, Department of Pharmacology, Nandha College of Pharmacy, Erode.

The work is original and has not been previously formed the basis for the award of any other Degree, Diploma, Associateship, Fellowship or any other similar title and the dissertation represent entirely an independent work on the part of the candidate.

Prof. Dr. S.Sengottuvelu, M. Pharm, Ph.D.,
Head, Department of Pharmacology,
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CERTIFICATE

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This work is original and has not been submitted in part or full for any other degree or diploma of this or any other university.

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EVALUATION CERTIFICATE

This is to certify that the work embodied in this thesis entitled, **"ANTIDIARRHOEAL ACTIVITY OF *KEDROSTIS FOETIDISSIMA* LEAF EXTRACT ON EXPERIMENTALLY INDUCED DIARRHOEA IN MICE"** submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai, was carried out by **Reg. No. 261425411** Department of Pharmacology, Nandha College of Pharmacy, Erode-52 for the partial fulfillment for the award of degree of "Master of Pharmacy" in Pharmacology under supervision and guidance of **Prof. Dr. S. Sengottuvelu, M.Pharm, Ph.D.,** Head, Department of Pharmacology.

This work is original and has not been submitted in part or full for any other degree or diploma of this or any other university.

Internal Examiner **External Examiner**

Convener of Examination

DECLARATION

The work presented in this thesis **"ANTIDIARRHOEAL ACTIVITY OF *KEDROSTIS FOETIDISSIMA* LEAF EXTRACT ON EXPERIMENTALLY INDUCED DIARRHOEA IN MICE"** was carried out by me in the department of pharmacology, under the direct supervision of **Prof. Dr. S. Sengottuvelu, M. Pharm, Ph.D.,** Head, department of pharmacology, Nandha College of Pharmacy and Research Institute, Erode- 52.

This work is original and has not been submitted in part or full for the award of any other degree or diploma of any university.

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ACKNOWLEDGEMENT

Develop an attitude of gratitude, and give thanks for everything that happens to you, knowing that every step forward is a step toward achieving something bigger and better than your current situation. Success of any project depends solely on support, guidance and encouragement received from the guide and well wishers".

It gives me immense pleasure and contentment to acknowledge and thank all those who in big ways and small have contributed for this effort.

It is my proud privilege to express my sincere thanks to my research guide **Prof**. **Dr. S.Sengottuvelu, M.Pharm, Ph.D.,** Head, Department of Pharmacology, Nandha College of Pharmacy Erode-52. I take this opportunity to express my heartfelt gratitude to my reverend guide. Her discipline, principles, simplicity, caring attitude and provision of fearless work environment will be cherished in all walks of my life. I am very grateful to her for valuable guidance and everlasting encouragement throughout my course.

It is proud to express my sincere thanks to my beloved principal **Dr. T. Siva Kumar, M.Pharm., Ph.D.,** Nandha College of Pharmacy, Erode, with a deep sense of gratitude for his encouragement, co-operation, kind suggestions and providing the best facilities during this work.

I am highly obliged to thank honorable **Thiru V. Shanmugan, B.Com.** Chairman and **Mr. S. Nandhakumar Pradeep, M.B.A.,** Secretary**,** Nandha College of Pharmacy, Erode-52**,** for providing me the required infrastructure to undergo my study.

I am highly indebted and thankful to **Dr. S. Haja sherief M. Pharm., Ph.D., Asst. Professor** Department of Pharmacology, Nandha College of pharmacy, Erode, for his painstaking support, unremitting encouragement and supportive guidance throughout my project work. His invaluable contributions made my work so simple and logical.

I am highly indebted and thankful to **Prof. Dr. R. Duraisami. M.Pharm., Ph.D.,** Head, Department of Pharmcognosy, Nandha College of pharmacy, Erode, for his painstaking support, unremitting encouragement and supportive guidance throughout my project work. His invaluable contributions made my work so simple and logical manner.

It's my sincere gratitude to thank my friend and **Mr. T. Karthick** for the help and encouragement during my postgraduate course to the completion of my thesis.

I would like to express my sincere thanks to librarians **Mrs. A. Sasikala and Mrs. P. Chitra** and lab attenders **Mrs Vijaya and Mrs. Kalaiselvi**.

The completion of this dissertation and my entire postgraduate course is not only fulfillment of my dream but also the dream of **my parents Mr. K. Vadivelu and Mrs. V. Mallika** who have been there for in every situation in my life again I say thank you. I would like also to thank who have been a great source of encouragement and motivation to me to be able to achieve every mile stone in my life. and I give special thanks to my friends and my co wokers.

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सं. भा.व.स./द.क्षे.के./No.: BSI/SRC/5/23/2015/Tech. /1789 दिनांक/Date: 16th November 2015

सेवा में / To

Siva Prakash.V
2nd Year M. Pharmacy
Department of Pharmacology
Nandha College of Pharmacy
Erode - 52

महोदय/Sir,

The plant specimen brought by you for identification is identified as Kedrostis foetidissima - CUCURBITACEAE. The identified specimen is returned herewith for preservation in their college/ Department/ Institution Herbarium.

धन्यवाद/Thanking you

भवदीय/Yours faithfully,

16/11/15

(डॉ. जी.वी.एस. मूर्ति /Dr. G.V.S. Murthy)
वैज्ञानिक 'एफ' एवं कार्यालय अध्यक्ष /
Scientist 'F' & Head of Office

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Committee for the Purpose of control and Supervision of Experiments on Animals (CPCSEA)
Institutional Animal Ethics Committee (IAEC)
Reg No: 688 /PO/Re/S/02/CPCSEA

CERTIFICATE

Title of the project	:	Antidiarrhoeal activity of kedrostis foetidissima whole plant extract on experimentally induced diarrhoea in mice
Proposal Number	:	NCP/IAEC/2015 – 16 – 01
Date received after modification (if any)	:	---
Date received after second modification	:	---
Approval date	:	24-12-2015
Species & Number of animals sanctioned	:	Wistar Albino mice-72
Expiry date (Termination of the Project)	:	15-07-2016
Name of the IAEC / CPCSEA Nominee	:	Prof. Dr. K. Balasubramanian

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Dr. R.PALANISAMY
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CONTENTS

1. INTRODUCTION

Diarrhoea is a condition of having three or more loose or liquid stools per day (Kasper *et al*., 2005). It is a common cause of death in Third World Countries and the second most known cause of children deaths worldwide (Weber, 1996; WHO, 2009). The loss of fluid and electrolytes through diarrhoea can cause dehydration and electrolyte imbalances. In 2009, diarrhoea was estimated to have caused 1.1 million deaths in people aged 5 years and over, and 1.5 million deaths in children under the age of 5 years. Oral rehydration solutions are the treatment of choice and have been estimated to have saved 50 million children in the past 25 years (Wilson, 2005). Diarrhoea due to infection, may last a few days or several weeks, as in persistent diarrhoea. Severe diarrhoea may be life threatening due to fluid loss in watery diarrhoea, particularly in infants and young children, the malnourished and people with impaired immunity. The impact of repeated or persistent diarrhoea on nutrition and the effect of malnutrition on susceptibility to infectious diarrhoea, can be linked to a vicious cycle amongst children, especially in developing countries. It is also associated with other infections such malaria and

measles. Chemical irritation of the gastrointestinal tract or non-infectious bowel disease can also result in diarrhoea (Kasper *et al*., 2005).

Diarrhoea is caused by a host of bacterial, viral and parasitic organisms most of which can be spread by contaminated water. It is more common where there is a shortage of clean water for drinking, cooking and cleaning, and basic hygiene is important in prevention. Water contaminated with human faeces, for example, from municipal sewage, septic tanks and latrines is of special concern. Animal faeces also contain micro-organisms that can cause diarrhoea. It can also spread from person to person, aggravated by poor hygiene. Food is another major cause of diarrhoea when it is prepared or stored in unhygienic conditions. Water can contaminate food during irrigation, and fish and seafood from polluted water may also contribute to the disease. Worldwide, around 1.1 billion people lack access to improved water and 2.4 billion people have no basic sanitation. These will increase susceptibility to diarrhoea (Kasper *et al*., 2005).

Types and causes of Diarrhoea

Secretory diarrhoea means that there is an increase in the active secretion, or there is an inhibition of absorption. There is little or no

structural damage. The most common cause of this type of diarrhoea is cholera which stimulates the secretions of fluids into the gastrointestinal tract (GIT) following an increase in salt secretion like sodium chloride. The increase in the fluid buildup in the GIT lumen stimulates peristalsis resulting in watery diarrhoea (King *et al*.,2003).

Osmotic diarrhoea occurs when too much water is drawn into the GIT lumen. This can be the result of malabsorption caused by pancreatic disease, in which the nutrients and salts like sodium chloride are left in the GIT lumen to pull in water. Osmotic diarrhoea can also be caused by osmotic laxatives used in the treatment of constipation.

Exudative diarrhoea occurs with the presence of blood or pus in the stools. This occurs with inflammatory diseases such as Crohn's disease or ulcerative colitis. Inflammatory diarrhoea occurs when there is damage to the mucosal lining, which leads to passive loss of protein rich fluids and a decreased ability to absorb these loss fluids. Features of all three types of diarrhoea can be found in this type of diarrhoea. This type of diarrhoea can be caused by bacterial, viral, parasitic infections or autoimmune problems such as inflammatory bowel syndrome. It can also be caused by tuberculosis, colon cancer and enteritis. Generally, if there is blood

visible in the stools, it is referred to as dysentery which is a symptom of bacterial invasion of the colon by a shigella organism (Kasper *et al*., 2005; Wilson, 2005).

Treatment of Diarrhoea

Most episodes of diarrhoea are acute and self limiting and may reflect food intolerance, bacterial toxin infection or enteric infection. The first line management is the prevention or treatment of fluid and electrolyte depletion. This is particularly important for infants, children and the frail elderly and may be achieved by either homemade or commercially available oral rehydration solutions (Kasper *et al*., 2005).

Drug treatment

Drugs may be used in the management of diarrhoea. The different kinds of antidiarrhoeal drugs include anti-propulsives, anti-infectives; intestinal absorbents and anti-inflammatory drugs.

Anti-propulsive

(1) Loperamide

Loperamide is an opioid-receptor agonist and acts on the μ-opioid receptors in the myenteric plexus of the large intestine; by itself it does not affect the central nervous system like other opioids. It works by

decreasing the activity of the myenteric plexus, which, like morphine, decreases the tone of the longitudinal smooth muscles but increases tone of circular smooth muscles of the intestinal wall. This increases the amount of time substances stay in the intestine, allowing for more water to be absorbed out of the feacal matter. Loperamide also decreases colonic mass movements and suppresses the gastrocolic reflex. It may also reduce gastrointestinal secretions. It is given by mouth as an antidiarrhoeal drug and as an adjunct in the management of acute or chronic diarrhoea and is usually obtainable as 2 mg tablets or 1 mg/5 ml syrup. About 40% of the dose of loperamide is reported to be absorbed from the gastrointestinal tract to undergo first-pass metabolism in the liver and excretion in the faeces via the bile inactive conjugate, there is slight urinary excretion. Little intact drug reaches the system circulation. The elimination half life is reported to be 1 hour (Altman, 2001; Waller *et al*., 2005)**.**

In acute diarrhoea, the usual dose for adults is 2 tablets immediately followed by 1 tablet after each loose stool to a maximum of 8 tablets per day, the usual daily dose is 3 to 4 tablets. In children the dose is 5 ml three to four times a day up to 3 days (SAMF, 2010).

In chronic diarrhoea, the usual dose for adults is 2 to 4 tablets daily in divided doses subsequently adjusted as necessary. The major side effects for loperamide are abdominal pain, bloating, nausea, dry mouth, dizziness, and fatigue and hypersensitivity reactions like skin rashes. Loperamide has been associated with paralytic ileus particularly in infants and young children and death has been reported. Depression of CNS, to which children may be more sensitive, may be seen in over dosage and naloxone hydrochloride has been recommended for its treatment (Martindale, 2005).

Loperamide should not be used when inhibition of peristalsis is to be avoided, in particular where ileus or constipation occurs, and should be avoided in patients with abdominal distension, acute inflammatory bowel disease or antibiotic-associated colitis. It should not be used alone in patients with dysentery because dysentery is caused by bacteria and therefore, an antibiotic use is necessary. Loperamide should be used with caution in patients with hepatic impairment because of its considerable first-pass metabolism in the liver and should not be used in infants. Concomitant use with co-trimoxazole increases the bioavailability of loperamide, apparently by inhibition of the first-pass metabolism

(Martindale 2005).It is considered safe for use by breast feeding mothers as there has not been any report of clinical effect on the infant associated with its use (Kasper *et al*., 2005).

(2) Diphenoxylate

Diphenoxylate hydrochloride is a synthetic derivative of pethidine with little or no analgesic activity. It reduces the intestinal motility and is used in the symptomatic treatment of acute or chronic diarrhea. It is well absorbed from the gastrointestinal tract and is rapidly and extensively metabolized in the liver principally to diphenoxylic acid, which has antidiarrhoeal activity. Other metabolites include hydroxydiphenoxylic acid. It is excreted mainly as metabolites and their conjugates in the faeces and lesser amounts in urine. It may be distributed in breast milk (Martindale, 2005).

In acute diarrhea, the usual dose for adults is 10mg by mouth followed by 5mg every 6 hours, later reduced as the diarrhoea is controlled. Suggested initial doses for children 4 to 8 years of age, are 2.5mg three times a day; 9 to 12 years, 2.5mg four times a day and over 12 years, 5mg three times a day. Similar initial doses are used for chronic diarrhoea and subsequently, reduced as necessary (SAMF, 2010).

Diphenoxylate is related to opioid analgesics and its adverse effects and their treatment are similar, particularly in overdosage. The reported side effects include anorexia, nausea, vomiting, abdominal distension or discomfort, paralytic ileus, toxic megacolon, pancreatitis, headaches, drowsiness, restlessness, euphoria, depression, numbness of extremities, angioedema, pruritus and swelling of the gums. Signs of overdosage may be delayed and patients should be observed for at least 48 hours. Young children are particularly susceptible to effects of overdosage.

The presence of subclinical dose of atropine in preparation containing diphenoxylate may give rise to the side effects of atropine, such as blurred vision, constipation, flushing, urinary retention, tachycardia, mental confusion and agitation, in susceptible individual or in overdosage, thereby, acting as a preventive measure to potential abuse.

Diphenoxylate hydrochloride should be avoided in patients with jaundice, intestinal obstruction; antibiotic associated colitis or diarrhoea associated with enterotoxin-producing bacteria and should be used with caution in patients with hepatic impairment. It should also be used with caution in young children because of a greater variability of response in this age group and is not generally recommended in infants. Patients with

inflammatory bowel disease receiving diphenoxylate should be carefully observed for signs of toxic megacolon and it should be discontinued immediately should abdominal distention occur. There is a theoretical risk of hypertensive crisis if it is used with monoamine oxidase inhibitors (MAOI's) due to its structural relationship with pethidine (Kasper *et al*., 2005; Wilson, 2005; Martindale, 2005).

TRADITIONAL HERBAL MEDICINE

By definition, 'traditional' use of herbal medicines implies substantial historical use, and this is certainly true for many products that are available as 'traditional herbal medicines'. In many developing countries, a large proportion of the population relies on traditional practitioners and their armamentarium of medicinal plants in order to meet health care needs. Although modern medicine may exist side-by-side with such traditional practice, herbal medicines have often maintained their popularity for historical and cultural reasons. Such products have become more widely available commercially, especially in developed countries. In this modern setting, ingredients are sometimes marketed for uses that were never contemplated in the traditional healing systems from which they emerged. An example is the use of ephedra

(= Ma huang) for weight loss or athletic performance enhancement (Shaw, 1998).

THE ROLE OF HERBAL MEDICINES IN TRADITIONAL HEALING

The pharmacological treatment of disease began long ago with the use of herbs (Schulz *et al*., 2001). Methods of folk healing throughout the world commonly used herbs as part of their tradition.

Traditional Chinese medicine has been used by Chinese people from ancient times. Although animal and mineral materials have been used, the primary source of remedies is botanical. Of the more than 12 000 items used by traditional healers, about 500 are in common use. Botanical products are used only after some kind of processing, which may include, for example, stir-frying or soaking in vinegar or wine. In clinical practice, traditional diagnosis may be followed by the prescription of a complex and often individualized remedy. Traditional Chinese medicine is still in common use in China. More than half the population regularly uses traditional remedies, with the highest prevalence of use in rural areas. About 5000 traditional remedies are

available in China; they account for approximately one fifth of the entire Chinese pharmaceutical market (Li, 2000).

Many herbal remedies found their way from China into the Japanese systems of traditional healing. Herbs native to Japan were classified in the first pharmacopoeia of Japanese traditional medicine in the ninth century (Saito, 2000).

Ayurveda is a medical system primarily practised in India that has been known for nearly 5000 years. It includes diet and herbal remedies, while emphasizing the body, mind and spirit in disease prevention and treatment (Morgan, 2002).

MEDICINAL APPLICATIONS, BENEFICIAL EFFECTS AND ACTIVE COMPONENTS

In some cases, the active principles of plant-derived products have been isolated and characterized, and their mechanisms of action are understood (e.g., ephedrine alkaloids in some species of Ephedra). For many, however, including virtually all of the most common products in the marketplace, such information is incomplete or unavailable. This is in large part due to the complexity of herbal and botanical preparations; they are not pure compounds. It is also a function of the traditionally-held

belief that the synergistic combination of several active principles in some herbal preparations is responsible for their beneficial effects.

WHO GUIDELINES FOR HERBAL MEDICINES

In 1992, the WHO Regional Office for the Western Pacific invited a group of experts to develop criteria and general principles to guide research work on evaluating herbal medicines (WHO, 1993). This group recognized the importance of herbal medicines to the health of many people throughout the world, stating: 'A few herbal medicines have withstood scientific testing, but others are used simply for traditional reasons to protect, restore, or improve health. Most herbal medicines still need to be studied scientifically, although the experience obtained from their traditional use over the years should not be ignored. As there is not enough evidence produced by common scientific approaches to answer questions of safety and efficacy about most of the herbal medicines now in use, the rational use and further development of herbal medicines will be supported by further appropriate scientific studies of these products, and thus the development of criteria for such studies'.

Table No: 1. Table shows various plants used for the treatment of diarrhea

S.No	PLANT NAME	PARTS USED	REFERENCE
1	*Alchornea cordifolia*	Leaf	Agbor *et al.,* 2004
2	*Aristolochia ringens*	Root	Adeyemi *et al.,* 2012
3	*Baphia nitida*	Leaves	Adeyemi and Akindele, 2008
4	*Calotropis gigantean*	Aerial part	Chitme, 2004
5	*Capparis zeylanica*	Leaf	Karanayil *et al*., 2011
6	*Carum copticum*	Seed	Balaji *et al.,* 2012
7	*Catharanthus roseus*	Leaf	Hassan *et al.,* 2011
8	*Cayratia Pedata*	Leaves	Karthik *et al.,* 2011
9	*Cinnamomum zeylanicum*	Bark	Rao and lakshmi , 2012
10	*Combretum sericeum*	Root	Sini *et al.,* 2008
11	*Coriandrum sativum*	Whole plant	Karmakar *et al.,* 2011
12	*Dalbergia lanceolaria*	Bark	Mujumdar *et al.,* 2005
13	*Delonix regia*	Flower	Shiramane *et al.,* 2011
14	*Ficus religiosa*	Stem bark	Panchawat and sisodia, 2012
15	*Geranium incanum Burm. f.*	Leaves	Amabeoku, 2009
16	*Hippocrataea Africa*	Root	Okokon *et al.,* 2011

17	*Hyptis siaveolens*	Leaves	Shaikat *et al.,* 2012
18	*Indigofera pulchra*	Aerial part	Mohammed *et al.,* 2009
19	*Ipomes obscura*	Leaf	Seshadri *et al*., 2007
20	*Ixora coccinea*	Flower	Maniyar *et al.,* 2010
21	*Murraya koenigii*	Leaves	Sharma *et al.,* 2012
22	*Pterocarpus erinaceus*	Leaf	Ezeja *et al.,* 2012
23	*Securinega virosa*	Leaves, root bark, stem	Magaji *et al*., 2007
24	*Strychnos potatorum*	Dried seeds	Biswas *et al.,* 2002
25	*Xanthium indicum*	Leaves	Akter *et al.,* 2009

2. PLANT PROFILE

Figure: 1 *Kedrostis Foetidissima*

BOTANICAL DESCRIPTION

- **Botanical Name :** *Kedrostis foetidissima*(Jacq.) Cogn
- **Class :** Dicotyledons
- **Subclass :** Polypetalae
- **Series :** Calyciflorae
- **Order :** Passiflorales
- **Family :** Cucurbitaceae
- **Genus :** *Kedrostis*
- **Species :** *Foetidissima*

VERNACULAR NAME

- **Tamil** **:** Appakovai
- **Telungu** **:** Kukumadumda / Nagadonda
- **Kannada** **:** Kukumadumdarnara
- **Bombay** **:** Nurakvels

Ecology And Distribution:

World wide in distribution. It is Rich in the regions of south Africa and Asia.

In India:

The *Kedrostis foetidissima* is Distributed in the warm and dry areas of Gujarat, Punjab, Uttarpradesh, Maharastra & Andhrapradesh and it is also found in the Malabar, Deccan and Carnatic regions of India.

Conservation:

Kedrostis foetidissima is a least concerned plant and is a threatened species it requires severe attention for conservation.

Cucurbitaceae:

The cucurbitaceae is essentially a tropical family containing 110 genera and 640 species. In India the family is represented by 37 genera and about 97 species several of which are cultivated throughout India.

Plant *kedrostis foetidissima* (jacq.) Cogn:

Scandent , Monoceious, Stem slender, Branched, angled, Sparsely hairy, Tendrils simple, Filiform, Glabrous.

Root :

In Kedrostis root is perennial due to presence of Root Stocks.

Stem:

It is slender distance between node and inter node 8.5 10.2 cm long.

Leaves:

Leaves are 5.8 cm long, 7.1 cm breadth and as broad as long membranous, arbicular in out line, bright green, hairy and more or less scab rid on both sides margins entire or distantly toothed, cordate at the base. Some time five angled are sublobate, the lobes sub acute, apiculate,

Petioles:

Petioles are 2.7-2.8 cm long, hairy.

Male Flower:

In male flower peduncles filiform 2.9 cm long, 0.7 mm at the apex, pedicles capillary 0.7 mm long usually bracteolate at the base, male flower length 0.7 mm across, in racemes. Calyx tube compunlate calyx length 0.3 mm, rounded at the base teeth minute. Corolla pale yellow. Segment oblong lanceolate, acute, 0.6 mm long pubescent, stamens 3 inserted in the middle of calyx tube filaments free anthers sub orbicular.

Female Flower:

In female flower Peduncles 1.3 cm long, beaked, pubescent, ovary oblong 0.9 mm long, petles are 0.6 mm long, calyx 0.2 mm style glabrous, stylar disc small stigma 3 fid. Flowers are flask shaped. 2 mm style glabrous, stylar disc small stigma 3 fid. Flower are flask shaped.

Fruit:

Fruit sub sessile, Deep red, about4.9 cm long and beaks are 0.6 mm breadth, hair of fruit 0.2 0.1 mm ovaid, tapering into a long narrow beak, pubescent.

Seed:

Seeds 4 mm long, ovaid, with a narrow sharp wing brown (Nirmala J and Pandian, 2013).

Traditional Uses:

The leaf juice of *Kedrostis foetidissima*, locally named as *Appakovai*, applied externally on joints cures diarrhoea in babies of 3-4 months. Medicinal use, preparation and administration modes of 299 plant species belonging to168 genera in 68 families medicinal plants of Bulamogi in Uganda shows a record , that *Kedrostis foetidissima*, wild herb, was used in treatment of diarrhoea and measles. Leaf infusion was taken in treating diarrhoea and leaf decoction was taken orally in the treatment of measles (Ragupathy, 2008 and Tabuti *et al*., 2003).

3. LITERATURE REVIEW

- Otenio *et al., 2008,* reported the use of *Kedrostis foetidissima,* which was one of the plant in multi plant extract used in the treatment of opportunistic infection.
- Otenio *et al.,* 2007, documented the medicinal herb *Kedrostis foetidissima* along with *P.vogelii*, recommended for further pharmacological test on HIV cases and for domestication to serve them from local extinction.
- Kamatenesi *et al.,* 2011, suggested the roots of *Kedrostis foetidissima (jacq.)cogn*. crushed, mixed in cold water is taken once a day for the treatment of Measles.
- Giday, 2001, renowned the use of whole plant of *Kedrostis foetidissima*, for curing chest pain and its leaves used as a traditional veterinary medicine in the treatment of ALOYE .
- An ethnodiagnostic study conducted by Ole-Miaron, 2003, reports *Kedrostis foetidissima (jacq.)cogn*., as a rare plant with a very unpleasant smell but cattle feed on intravenously. The leaves are crushed and fed to cattle suffering from pasture bloat and frothy bloat.

- Priyavardhini *et al.,* 2008, reported the antibacterial activity of chloroform extract of leaf and stem of *Kedrostis foetidissima* against bacteria like *Streptococcus aureus, Escherichia coli, Pseudomonus aeruginosa, Klebsiella pneumonia, Serratia marcescens.*
- Otenio *et al.,* 1998, reported the aqueous extract of *Kedrostis foetidissima* was active against the measles virus *Leishmania denovani, the visceral Leishmania Parasite, as well as Trypanosoma brucei.*
- Choene and Motadi, 2012, explained the Anti-proliferative effects of the methanolic extract of *kedrostis foetidissima* in breast cancer cell lines.
- Amutha and Lalitha, 2013, studied the wound healing activity of Leaf and Stem Extract of *Kedrostis Foetidissima.*

4. AIM AND OBJECTIVE OF THE STUDY

Aim of the Study

Aim of the study is to screen the anti-diarrhoeal activity of ethanolic leaf extract of *kedrostis foetidissima* in mice.

Objective of the Study

Diarrhoea is common disease annually about 4 to 5 million diarrhoeal deaths occur in the developing countries through out the world (Senthil Nagaraj D *et al*., 2013). Now drug available in market for diarrhoea has variety of side effect. So there is need for a continuing search for effective anti-diarrhoeal drugs without side effect.

In recent years, the interest in plant-based medicine has increased worldwide. *kedrostis foetidissima* have many therapeutic uses in the practice of traditional medicine. This herb has been used to treat a number of disorders including inflammation, malaria, fever, worms, pain, diuresis, cancer, abortion, and various gastro-intestinal disorders. There is no scientific evidence on the antidiarrheal activity of *kedrostis foetidissima*. Hence, the present study was designed to evaluate the claims of the native practitioners.

5. PLAN OF THE WORK

1. Collection of Plant Material.

2. Authentication of Plant.

3. Extraction of plant material by maceration method using ethanol.

4. Preliminary phyto-chemical analysis.

5. Ethical consideration.

6. Pharmacological evaluation

   - Measurement of faecal output
   - Castor oil model
   - Gastrointestinal transit test.

7. Statistical Analysis.

6. MATERIALS AND METHODS

Plant Material

Collection and Authentication

The leaves of *Kedrostis foetidissima* was collected from Kolli hills. It was identified and authenticated as *Kedrostis foetidissima* by Scientist 'F' Botanical survey of India, Southern Regional Centre, Tamilnadu Agriculture University, Coimbatore. The voucher specimen (BSI/SRC/5/23/2015/Tech/1789) has been deposited in department for further references.

Preparation of Extract

The collected leaves were, shade dried and then ground into coarse powder. The powder was then subjected to exhaustive extraction by a maceration process using 90% ethanol as a solvent at room temperature for 7 days. The ethanolic extract was concentrated by vacuum distillation to dry. The collected extract was stored in desiccators and used for further pharmacological study.

Phytochemical Analysis (CK Kokate1994, Harsone 2007)

A systematic and complete study of crude drugs includes a complete investigation of both primary and secondary metabolites derived from plant metabolism. Different qualitative test were performed for establishing profiles of various extracts for their nature of chemical composition. The extracts obtained were subjected to following chemical tests for identification of various phytoconstituents as per the methods given by Harborne. There were no previously isolated compounds.

1. TEST FOR STEROLS

a. Salkowski test: Few drops of concentrated sulphuric acid was added to the chloroform solution, shaken and allowed to stand, appearance of red color in lower layer indicates the presence of sterols.

b. Liebermann-Burchard test: To the chloroform solution, few drops of acetic anhydride was added and mixed well. 1 mL of concentrated sulphuric acid was added from the sides of the test tube, appearance of reddish brown ring indicates the presence of sterols.

2. TEST FOR TRI-TERPENES

a. Salkowski test: Few drops of concentrated sulphuric acid was added to the chloroform solution, shaken and allowed to stand, appearance of golden yellow color indicates the presence of triterpenes.

b. Liebermann-Burchard test: To the chloroform solution, few drops of acetic anhydride was added and mixed well. 1 mL of concentrated sulphuric acid was added from the sides of the test tube, appearance of deep red color indicates the presence of triterpenes.

3. TEST FOR SAPONINS

a. Foam test: Small amount of extract/ fraction was shaken with little quantity of water, if foam produced persists for 10 minutes; it indicates the presence of saponins.

b. Haemolysis test: To 2 mL of 1.8% sodium chloride solution in two test tubes, 2 mL distilled water was added to one of the test tube and to other 2 mL of 1% sample extract/ fraction was added. 5 drops of blood was added to each test tube and gently mixed the contents. Haemolysis was observed under the microscope on glass slide, indicates the presence of saponins in the extract.

c. Froth test: To 5 ml of extract of the drug added a drop of sodium bicarbonate solution. Shaken the mixture vigorously and left for 3 minutes. Honey comb like froth is formed.

4. TEST FOR ALKALOIDS: The various extract/ fractions were basified with ammonia and extracted with chloroform. The chloroform solution was acidified with dilute hydrochloric acid. The acid layer was used for testing the alkaloids.

a. Wagner's test (Iodine in Potassium iodide): The acid layer was treated with few drops of Wagner's reagent. Formation of reddish brown precipitate indicates the presence of alkaloids.

b. Mayer's test (Potassium Mercuric Iodine solution): The acid layer was treated with few drops of Mayer's reagent. Formation of creamy white precipitate indicates the presence of alkaloids.

c. Dragendorff's reagent (Potassium Bismuth Iodide): The acid layer was treated with few drops of Dragendorff's reagent. Formation of reddish brown precipitate indicates the presence of alkaloids.

d. Hager's test: The acid layer was treated with few drops of Hager's reagent. Formation of yellow precipitate indicates the presence of alkaloids.

5. TEST FOR CARBOHYDRATES: Small amount of extracts/ fractions were dissolved in little quantity of distilled water and filtered separately. The filtrates were used to test presence of carbohydrates.

a. Molisch's test: The extract was treated with Molisch reagent and concentrated sulphuric acid was added from the sides of the test tube to form a layer. A reddish violet ring shows the presence of carbohydrates.

b. Fehling's test: Filtrates were hydrolyzed with dilute hydrochloric acid, neutralized with alkali and heated with equal amount of Fehling's A and B solutions. Formation of green to yellow to red precipitate indicated the presence of reducing sugars.

c. Barfoed's test: To the filtrate few drops of Barfoed's reagent was added and boiled in water bath. Brick red precipitate formation shows the presence of carbohydrates.

d. Benedict's test: to the filtrate added 2 mL Benedict's reagent and boiled in water bath. Green reddish brown precipitate is formed.

6. TEST FOR TANNINS

a. Ferric chloride test: To extracts a few drops of 1% neutral ferric chloride solution was added, formation of blackish blue color indicates the presence of tannins.

b. Gelatin test: To the extracts added 1% solution of gelatin containing 10% sodium chloride. Formation of white precipitate indicates the presence of tannins.

7. TEST FOR FLAVONOIDS

a. Shinoda test: To the alcoholic solution of extract a few fragments of magnesium ribbon and concentrated hydrochloric acid was added. Appearance of red to pink color after few minutes indicates the presence of Flavonoids.

b. Ferric chloride test: Few drops of neutral ferric chloride solution were added to little quantity of alcoholic extract. Formation of blackish green color indicates the presence of phenolic nucleus.

c. Lead acetate test: To the extract, a few drops of aqueous basic lead acetate solution were added. Formation of yellow precipitate indicates presence of flavonoids.

d. Zinc-hydrochloric acid reduction test: The alcoholic solution was treated with a pinch of zinc dust and few drops of concentrated hydrochloric acid. Formation of magenta color after few minutes indicates the presence of flavonoids.

e. Alkaline reagent test/ NaOH test: To alcoholic solution added few drops of sodium hydroxide solution. Intense yellow color which disappeared after adding dilute HCl indicates the presence of flavonoids.

8. TEST FOR LACTONES

a. Legal test: The extract was dissolved in pyridine and a mixture of sodium nitroprusside and sodium hydroxide was added. Deep red color indicates the presence of lactones.

b. Baljet test: To the extract, sodium picrate solution was added. Formation of yellow color indicates the presence of lactones.

9. TEST FOR AMINO ACID/ PROTEIN

a. Ninhydrin test: Heated the 3 mL of extract and 3 drops of ninhydrin solution in boiling water bath for 10 minutes. Appearance of purple color shows the presence of amino acids.

b. Biuret test: To 3 mL of extract added 4% NaOH and few drops of 1% cooper sulphate solution. Formation of violet color confirms the presence of protein.

c. Millon's reagent test: Mixed the extract with millon's reagent. Formation of brick red precipitate indicates the presence of protein.

d. Xanthoproteic test: To 1 mL of concentrated nitric acid was added boiled for 1 minute and liquid ammonia was added. Precipitate is formed.

10. TEST FOR RESINS: Dissolved the extract in acetone and pour the solution in to distilled water. Turbidity indicates the presence of resins.

11. TEST FOR STARCH: dissolved 0.015 gm of iodine and 0.075 gm of potassium iodide in 5 mL of distilled water and add 2-3 mL of an aqueous extract of drug, blue color is produced.

Animals

Wistar albino mice (20 – 25 gm) were used for the study. The animals were obtained from animal house, Nandha College of Pharmacy, Erode. The animals were placed at random and allocated to treatment groups in polypropylene cages with paddy husk as bedding. Animals were housed at a temperature of 24±2^{o}C and relative humidity of 30 – 70 %. A 12:12 light:day cycle was followed. All animals were allowed to free access to water and fed with standard commercial pelleted rat chaw (M/s. Hindustan Lever Ltd, Mumbai). All the experimental procedures and protocols used in this study were reviewed and approved by the Institutional Animal Ethics Committee of Nandha College of Pharmacy (Reg No: 688 / PO/Re/S/02 / CPCSEA) and were in accordance with the guidelines of the CPCSEA.

Anti-diarrheal Activity

Measurement of faecal output

Faecal output was measured following the methods of Pillai (1992). Four groups of mice (n = 6) were housed singly in separate cages. Group I served as the control and received 0.1% CMC (Carboxy Methyl Cellulose solution). Groups II & III mice were treated respectively with

200 & 400 mg/kg of extract, while group IV mice received Loperamide at 5 mg/kg, p.o., the standard anti-diarrhoeal drug. Following treatment, the faecal materials were collected for 8 h post treatment, were dried in an incubator and their weights measured. The percentage faecal output (%FOP) was calculated as follows:

$$\% FOP = \frac{f_t \times 100}{f_c}$$

where, f_t , is the mean faecal weight of each treatment group, and f_c is that of control group (Akah *et al.,* 1999).

Castor oil model Otshudi *et al.* (2001)

Overnight-fasted mice were randomly divided into four groups (n = 6). Group I served as the control and received 0.1% CMC (Carboxy Methyl Cellulose solution; Groups II & III mice were treated respectively with 200 & 400 mg/kg of *Kedrostis foetidissima* extract, while group IV mice received Loperamide at 5 mg/kg, p.o., the standard anti-diarrhoeal drug. 1 h later, diarrhoea was induced in all groups by inoculating castor

oil (0.5 ml/mouse, p.o.). The numbers of diarrhoeal episodes were recorded for each time and cumulative values were calculated for 4 h post induction of diarrhoea, and the numbers of animals devoid of diarrhoeal droppings at 4 h were considered as a percentage protection from diarrhoea.

Gastrointestinal transit test

The animals were starved for 16 h prior to the experiment. Group I served as the control and received 0.1% CMC (Carboxy Methyl Cellulose solution; Groups II & III mice were treated respectively with 200 & 400 mg/kg of *Kedrostis foetidissima* extract, while group IV mice received Loperamide at 5 mg/kg, p.o., the standard anti-diarrhoeal drug. 5 min later, 0.5 ml of charcoal meal was orally inoculated to each mouse. All the mice were sacrificed 30 min later, their small intestines from pylorus to caecum cut out and distance travelled by the charcoal marker measured, and expressed as a percentage of the total length of small intestines. The percentage inhibition of the marker transit in the intestine was calculated as described by Akah & Offiah (1992).

Statistical Analysis

Results were expressed as mean ± SEM. The data were analyzed by using one way analysis of variance (ANOVA) followed by Dunnet's t test. P values < 0.05 were considered as significant.

7. RESULTS

Table No:2. Qulitative Phytochemical Analysis of Ethanolic extract of *Kedrostis foetidissima* leaves

S.No	Plant constituents	*Kedrostis foetidissima* leaf Extract
1	Test for sterols	+
2	Test for tri terpenoids	+
3	Test for saponins	+
4	Test for alkaloids	-
5	Test for carbohydrates	+
6	Test for tannins	+
7	Test for flavonoids	+
8	Test for lactones	-
9	Test for amino acid and proteins	-
10	Test for resins	+
11	Test for starch	-

+Present
- Absent

The result of phytochemical analysis as shown on table. the phytochemical analysis reveals the presence of sterols, tri terpenoids, saponin, carbohydrates, tannins, flavonoids, resins of ethanolic leaf extract of *Kedrostis foetidissima.*

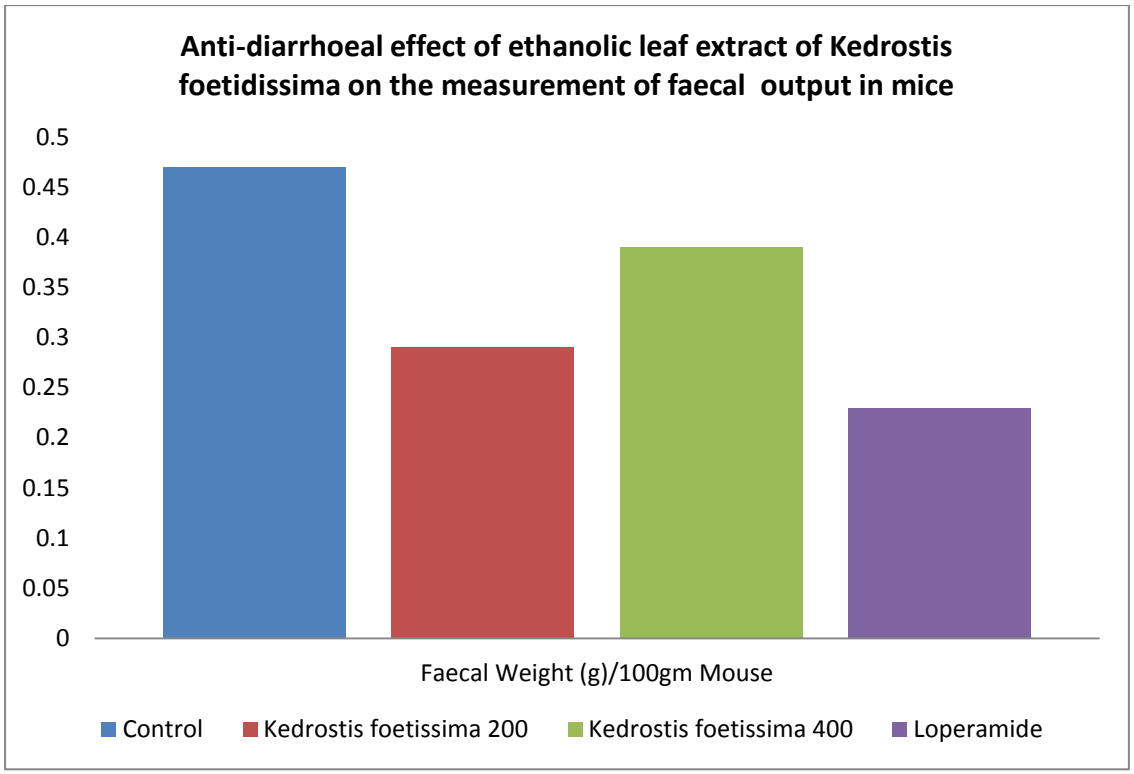
Anti-diarrheal Activity

Measurement of faecal output

Table No:3. The table shows the anti-diarrhoeal effect of ethanolic leaf extract of *Kedrostis foetidissima* on the measurement of faecal output in mice

S.No	Drug Treatment	Faecal Weight (g)/100 gm Mouse	% Reduction
1	Control (0.1% CMC)	0.47 ± 0.02	-
2	*Kedrostis foetidissima* (200mg/kg)	0.29±0.01***	51.06
3	*Kedrostis foetidissima* (400mg/kg)	0.39±0.02*	38.29
4	Reference Control Loperamide (5mg/kg)	0.23 ±0.01**	17.01

Values are in mean ± SEM (n=6),
*P<0.05 , **P<0.01, ***P<0.001 Vs Control

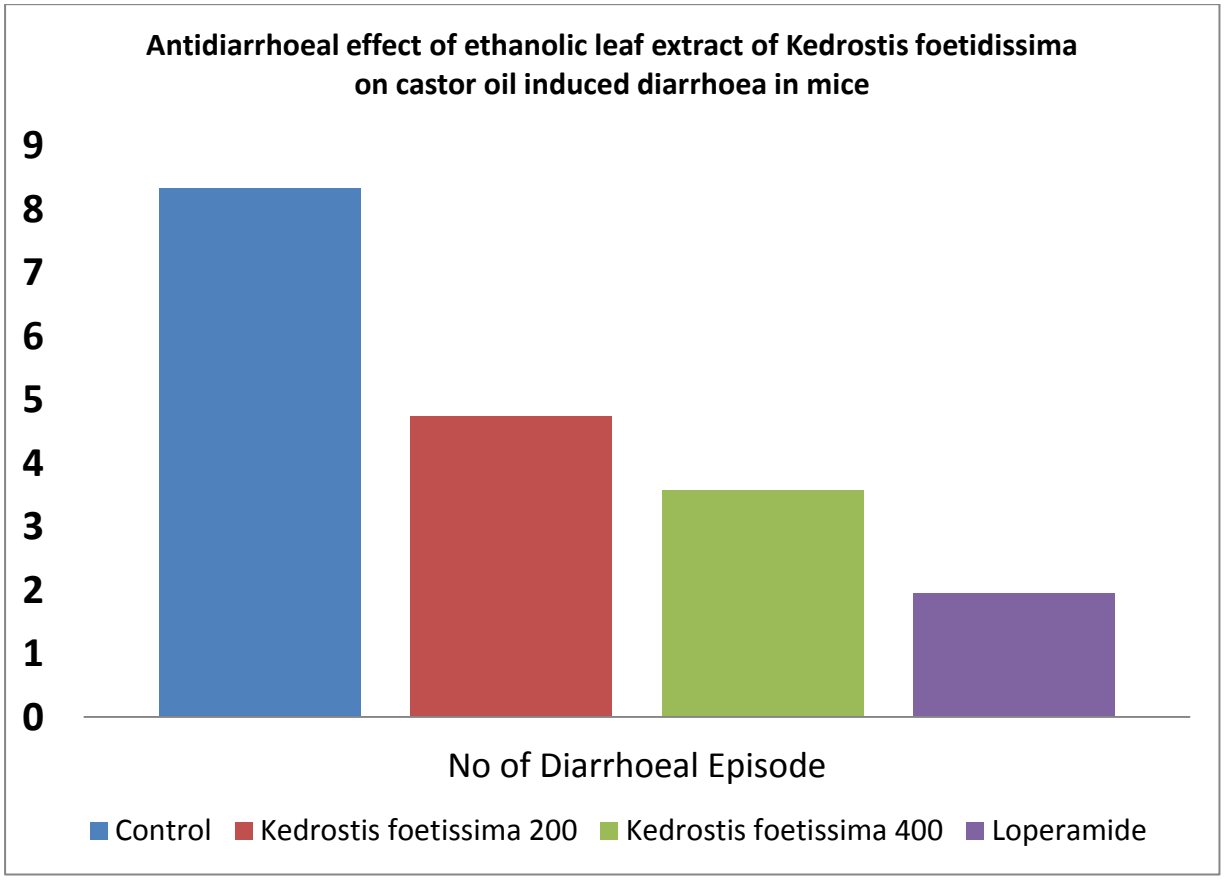

Anti-diarrhoeal effect of ethanolic leaf extract of Kedrostis foetidissima on the measurement of faecal output in mice
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
Faecal Weight (g)/100gm Mouse
Control
Kedrostis foetissima 200
Kedrostis foetissima 400
Loperamide

The anti-diarrhoeal activity of ethanolic leaf extract of *Kedrostis foetidissima* was studied using mice by faecal output method and the result was shown on table 3. Treatments of *Kedrostis foetidissima* leaf extract at 200 & 400 mg/kg, p.o. doses could reduce faecal production of the treated mice significantly in a dose-dependant manner. The faecal weight of control group was 0.47 ± 0.02 g/100gm animal. The faecal weight of *Kedrostis foetidissima* leaf extract 200 and 400 mg/kg was 0.29 ±0.01 and 0.39±0.02 g/100gm animal respectively. The faecal output of the reference control loperamide was 0.23 ±0.01 g/100gm animal. The % reduction in faecal output was recorded to be 51.06 and 38.29 for the extract (200 & 400 mg/kg, respectively) and Loperamide it was 17.01 %.

Table No: 4. The table shows the anti-diarrhoeal effect of ethanolic leaf extract of *Kedrostis foetidissima* on castor oil induced diarrhoea mice.

S.No	Drug Treatment	No of Diarrhoeal Episodes at 4 hrs	% Reduction
1	Control (0.1% CMC)	8.32±0.03	-
2	*Kedrostis foetidissima* (200mg/kg)	4.73±0.02**	43.15
3	*Kedrostis foetidissima* (400mg/kg)	3.56±0.01**	57.21
4	Reference Control Loperamide (5mg/kg)	1.95±0.01***	76.56

Values are in mean ± SEM (n=6),
*P<0.05 , **P<0.01, ***P<0.001 Vs Control

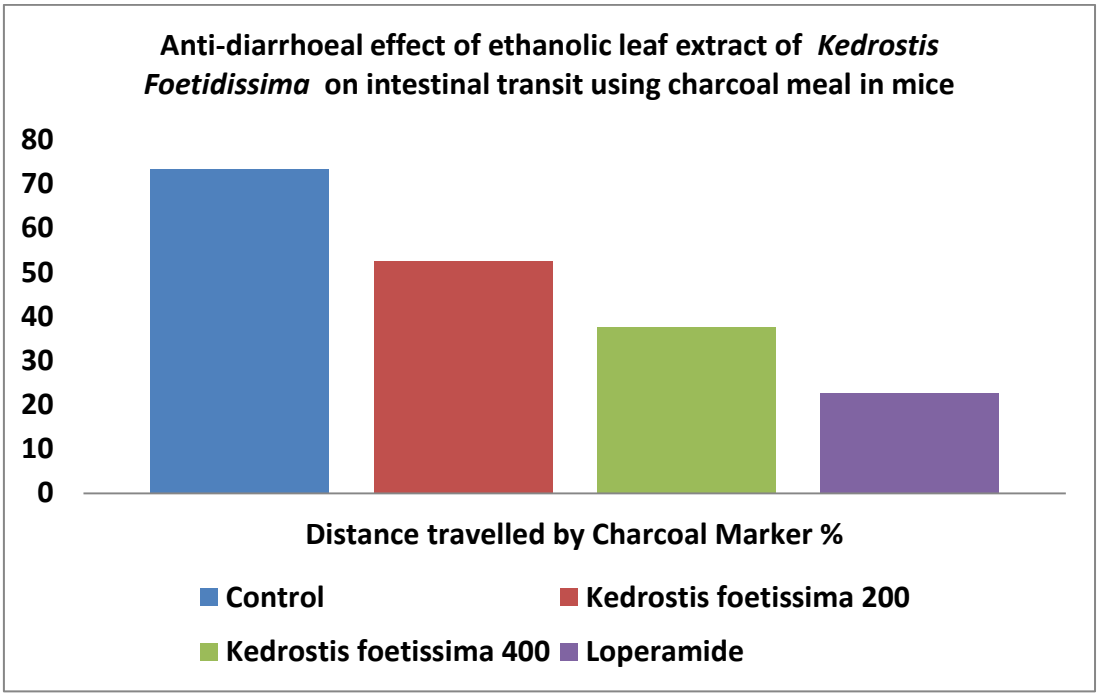

Antidiarrhoeal effect of ethanolic leaf extract of Kedrostis foetidissima on castor oil induced diarrhoea in mice
9
8
7
6
5
4
3
2
1
0
No of Diarrhoeal Episode
Control
Kedrostis foetissima 200
Kedrostis foetissima 400
Loperamide

The anti-diarrhoeal activity of ethanolic leaf extract of *Kedrostis foetidissima* was studied using mice by castor oil induced diarrhoea and the result was shown on table 4. Treatments of *Kedrostis foetidissima* leaf extract at 200 & 400 mg/kg, p.o. doses could reduce number of diarrhoeal episodes of the treated mice significantly in a dose-dependant manner. The number of diarrhoeal episode of control group was 8.32 ± 0.03. The number of diarrhoeal episode of *Kedrostis foetidissima* leaf extract 200 and 400 mg/kg was 4.73 ± 0.02 and 3.56 ± 0.01 respectively. The number of diarrhoeal episode of the reference control loperamide was 1.95 ± 0.01. The % reduction in faecal output was recorded to be 43.15 % and 57.21 % for the extract (200 & 400 mg/kg, respectively) and Loperamide it was 76.56 %.

Table No: 5. The table shows the anti-diarrhoeal effect of ethanolic leaf extract of *Kedrostis foetidissima* on intestinal transit using charcoal meal in mice.

S.No	Drug Treatment	Distance travelled by Charcoal Marker (%)
1	Control (0.1 % CMC)	73.32
2	*Kedrostis foetidissima* (200mg/kg)	52.51**
3	*Kedrostis foetidissima* (400mg/kg)	37.63***
4	Reference Control Loperamide (5mg/kg)	22.56***

Values are in mean ± SEM (n=6),
*P<0.05 , **P<0.01, ***P<0.001 Vs Control


Anti-diarrhoeal effect of ethanolic leaf extract of *Kedrostis Foetidissima* on intestinal transit using charcoal meal in mice
80
70
60
50
40
30
20
10
0
Distance travelled by Charcoal Marker %
Control
Kedrostis foetissima 200
Kedrostis foetissima 400
Loperamide

The anti-diarrhoeal activity of ethanolic leaf extract of *Kedrostis foetidissima* was studied by intestinal transit method using charcoal meal in mice and the result was shown on table 5. Treatments of *Kedrostis foetidissima* leaf extract at 200 & 400 mg/kg, p.o. doses significantly reduced the % of distance travelled by the charcoal marker in dose-dependant manner. The distance travelled by the charcoal marker in control group was 73.32 %. The same for *Kedrostis foetidissima* leaf extract 200 and 400 mg/kg was 52.5 % and 37.63 % respectively. The reference control loperamide showed 22.56 %.

8. SUMMARY

Diarrhoea accounts for more than 5-8 million deaths worldwide each year in age less than 5 years especially in developing countries. To combat this problem the world health organization has initiated a diarrhoea disease control program to study traditional medicine practices and other related aspects together with the evaluation of health education and prevention approaches. Plants have been a valuable source of natural product for maintaining human health for many years. About 80% of individuals from developed countries receive traditional medicines including compounds derived from medicinal plants. Such medicinal plants can e exploited since it has been shown that they are important sources of new chemical substances with potential therapeutic effects. *Kedrostis foetidissima* belonging to the family, Curcubitaceae, traditionally used for the treatment of diarrhoea in children. So far no scientific evidence available for its antidiarrhoeal potential, so effort has been taken to prove its traditional claim by screening the antidiarrhoeal activity of ethanolic leaf extract of *Kedrostis foetidissima* in mice. Phytochemical analysis was carried for the ethanolic leaf extract which shows the presence of tannins, terpenoids, flavanoids. Adult Wistar

albino mice were used in the study for evaluating the antidiarrhoeal acitivity. Well established antidiarrhoeal models like Measurement of faecal output, Castor oil induced diarrhoea and charcoal meal induced gastrointestinal transit test were performed. For above test, the animals were divided into 4 groups of six animals each. Group I served as control received CMC solution, Group II and III were administered with 200 and 400 mg/kg of ethanolic leaf extract of *Kedrostis foetidissima* respectively. Group IV served as reference control, received 5mg/kg of Loperamide. The result showed that, in measurement of faecal output there was significant decrease in feacal out was observed with *Kedrostis foetidissima*, in castor oil induced diarrhoea test, both the doses of *Kedrostis foetidissima* reduced the number of diarrhoeal episodes and in charcoal meat test, there was significant decrease in % of distance travelled by the charcoal marker in dose-dependent manner. From the above it was concluded that, ethanolic leaf extract of *Kedrostis foetidissima* exhibited antidiarrhoeal activity in animal models.

9. CONCLUSION

From the present research work, it is concluded that the ethanolic leaf extract of *Kedrositis foetidissima* selected for pharmacological screening with a special reference to anti-diarrhoeal activity. Traditionally the leaves of *Kedrositis foetidissima* was used to control diarrhoea. Literature review on *Kedrositis foetidissima* reveals the plant possess antimicrobial, antitumor and wound healing activity. Phytochemical analysis shows the presence of triterpeniods saponins, carbhohydrates, tannins, flavanoids , resins, sterols etc. *Kedrositis foetidissima leaf extract* exhibited anti-diarrhoeal property in dose dependent manner in three different models. Further study has to be conducted by isolating the active principal responsible for anti-diarrhoeal property which may add a new herb anti-diarrhoeal agent**.**

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